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REMARKS

Claims 1-4 are all the claims pending in the application; claims 2-4 have been withdrawn from consideration; claim 1 has been rejected.

The specification has been amended to correct an obvious error in the ATCC deposit serial number, and update the address for the ATCC. Support for the correction to the deposit number may be seen in every other occurrence of the number in the specification.

Claim 1 has been amended to remove extraneous information.

New claims 5-49 have been added.

The ranges of increase in maytansinoid production recited in the new claims find support in the specification as follows. A 1.2-fold increase is a comparison between the highest level of maytansinoid production by the parental strain ATCC 31565, colony 15-55, reported in Table 4 (page 10), which is 221 mg/L of ansamitocin P-3, and the lowest level of production of a sample of the mutant strain PF4-4 of the present invention recorded in Table 5 (page 13), i.e., 268 mg/L. 268 mg/L divided by 221 mg/L gives a 1.2-fold increase.

Similarly, a 1.8-fold increase is a comparison between the highest level of maytansinoid production by the parental strain ATCC 31565, colony 15-55, reported in Table 4 (page 10), which is 221 mg/L of ansamitocin P-3, and the highest level of production of a sample of the mutant strain PF4-4 of the present invention reported in Table 5 (page 13), namely 401 mg/L. 401 mg/L divided by 221 mg/L gives a 1.8-fold increase.

The range of "5-fold to 10-fold" finds support in the specification at page 4, line 14.

Support for the *Actinosynnema pretiosum* strains, *Actinosynnema* strains and bacterial strains recited in the claims may be found at page 5, lines 7-9, and throughout the Background section of the specification.

Support for *Actinosynnema pretiosum* strains having ATCC accession numbers 31281 and 31309 may be found at page 2, lines 13-22.

Support for methods of making ansamitocins may be found at page 14, lines 1-13, Figure 2, and Example 3.

Support for methods of making an enhanced bacterial strain may be found at page 10, line 9, through page 12, line 8, and in Examples 1 and 2.

New claims 5-11, 16-20, 25-29, and 42-49 recite bacteria, and thus should be included in Group I, with regard to the restrictions requirement set forth in the Office Action dated August 9, 2002, in this application.

New claims 12-15, 21-24, and 30-33 recite methods of producing ansamitocins, and thus should be included in Group II, with regard to the restriction requirement.

No new matter has been added. Entry of this amendment is respectfully requested.

I. Claim Rejection – 35 U.S.C. §112

A. At paragraph 4A of the Office Action, claim 1 is rejected under 35 U.S.C. §112, first paragraph, as being non-enabled.

The Examiner states that the specification does not provide a repeatable method for obtaining the microorganism recited in the rejected claim, nor does the microorganism appear to be readily available. The Examiner notes that if the strain has been deposited under the terms of

the Budapest Treaty, a declaration by Applicants that all restrictions on the deposit will be irrevocably removed upon the granting of a patent would satisfy the enablement requirements.

In response, Applicants note that claim 1 recites a group of bacteria, and not one particular isolate. Therefore, the enablement of the claim should depend on the methods taught in the specification. Applicants note that the methods for producing a microorganism, having the biological characteristics of PF4-4, are clearly set forth in the specification (page 10, line 9, through page 11, line 12; page 18, line 1, through page 19, line 11). In view of the fact that the full scope of claim 1 is enabled, Applicants respectfully request reconsideration and withdrawal of this rejection.

On a related topic, Applicants note that included herewith are additional claims to be added to the application. Claim 5 recites mutant strain PF4-4 (ATCC PTA-3921). Also included herewith is an executed Statement of Availability, stating that all restrictions on the deposit of ATCC PTA-3921 will be irrevocably removed upon the granting of a patent. In view of the Statement, Applicants assert that new claim 5 is fully enabled.

B. At paragraph 4B of the Office Action, claim 1 is rejected under 35 U.S.C. §112, first paragraph, because the best mode for practicing the invention has not been disclosed.

In response, Applicants assert that the best mode for producing the microorganisms recited in claim 1 is disclosed in the specification at page 10, line 9, through page 11, line 12, and at page 18, line 1, through page 19, line 11. Further, as discussed above, this disclosure enables the full scope of claim 1. "It is, of course, fundamental that a patentee need disclose only the best mode conceived by him for practicing the invention, not all conceivable modes. To

require otherwise would place an unreasonable burden on the patentee, a burden not required by 35 U.S.C. §112.” *In re Marzocchi and Horton*, 169 USPQ 367, 169 (CCPA 1971).

As Applicants have provided the best mode for practicing the invention, reconsideration and withdrawal of this rejection is respectfully requested.

C. At paragraph 4C of the Office Action, claim 1 is rejected under 35 U.S.C. §112, first paragraph, as being non-enabled.

The Examiner asserts that while the specific microorganism is enabled (upon submission of a Statement of Availability), the broad scope of the claim is not enabled.

In response, Applicants note that this claim is limited to only those bacteria that have the biological characteristics of strain PF4-4 (ATCC PTA-3921).

Thus, the bacteria encompassed within the scope of the claim are *Actinosynnema pretiosum*. Furthermore, each bacterium encompassed by the claim has the ability to produce amounts of maytansinoids comparable to that of strain PF4-4.

The skilled artisan would easily be able to determine whether a candidate microorganism falls within the scope of the claim by determining whether the candidate is a strain of *Actinosynnema pretiosum* and produces comparable amounts of maytansinoids as strain PF4-4.

On this basis, Applicants assert that the claim is fully enabled, and respectfully request reconsideration and withdrawal of this rejection.

II. Claim Rejection – 35 U.S.C. §101

At paragraph 5 of the Office Action, claim 1 is rejected under 35 U.S.C. §101 as being a product of nature.

In response, Applicants note that as each of the bacteria encompassed within the scope of the claim must produce 5- to 10-fold more maytansinoid than the wild-type strain of *Actinosynnema pretiosum* ATCC 31565, and such enhanced producers have not been shown to be naturally occurring, it is clear that the bacteria of claim 1 are not a product of nature, and that the hand of man is involved.

Thus, as the claim does not include a product of nature, Applicants respectfully request reconsideration and withdrawal of this rejection.

III. Claim Rejection – 35 U.S.C. §102

At paragraph 6 of the Office Action, claim 1 is rejected under 35 U.S.C. §102 as being anticipated by Hasegawa et al. (USP 4,331,598) for ATCC 31565 or Hasegawa et al. (USP 4,450,234) for ATCC 15005.

The Examiner states that both of the strains disclosed in the two references are considered to be within the scope of the broad claim terminology as they have the same biological characteristics as claimed for the bacterium recited in claim 1.

In response, Applicants first note that the catalog page included by the Examiner with the office action for ATCC 31565 describes this microorganism as having the ability to produce maytansinoids. This strain is also noted in the specification as being the parental strain from which the PF4-4 strain of the present invention was produced.

As shown in Table 4, at page 10 of the specification, however, isolates of ATCC 31565 have only been identified that produce up to 221 mg/L of ansamitocin P-3. Claim 1 requires that bacteria falling within the scope of the claim produce levels of maytansinoid comparable to that of PF4-4. As shown in Figure 5, at page 13 of the specification, PF4-4 produces approximately 346 mg/L ansamitocin P-3 (the average of the three values that shown for PF4-4 in Table 5). Thus, ATCC 31565 does not meet each limitation of claim 1 as it does not produce a comparable level of maytansinoid as PF4-4.

As to ATCC 15005, the Examiner did not include the corresponding catalog page for this microorganism with the Office Action. Therefore, Applicants conducted a search of the ATCC website, and found that the microorganism assigned ATCC catalogue number 15005 is not one that produces a maytansinoid (a copy of the catalogue page is enclosed herewith for the Examiner's convenience).

Applicants also reviewed the 4,450,234 patent, listed by the Examiner as corresponding to ATCC 15005, and found that it claims the ATCC 31565 bacteria. Therefore, the identity of the second organism cited by the Examiner is unclear to Applicants. Applicants respectfully request the Examiner to provide a further explanation on this point of the rejection, and note that any further office action should be non-final as the present office action was not complete.

In view of the points discussed above, the subject matter of the pending claims is clearly not anticipated by the prior art and Applicants respectfully request reconsideration and withdrawal of this rejection.

IV. Rejoinder

Applicants note that under 35 U.S.C. §103(b)(i), a biotechnological process using or resulting in a composition of matter that is novel under §102 and non-obvious under §103(a) shall be considered non-obvious if claims to the process and the composition of matter are contained in the same application. In other words, if claims to the bacteria of claim 1 (and newly added claims 5-11, 16-20, 25-29, and 42-49), elected in response to the restriction requirement, are allowed, Applicants may request allowance of claims to the methods of using the bacterium (claims 2-4, and newly added claims 12-15, 21-24, and 30-33) and such claims should automatically be allowed.

Therefore, Applicants hereby assert that they wish to proceed under 35 U.S.C. §103(b)(i) and have claims to a method of using the bacterium found allowable (claims 2-4, and newly added claims 12-15, 21-24, and 30-33) if the bacteria of claim 1 (and newly added claims 5-11, 16-20, 25-29, and 42-49) is found allowable.

IV. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

AMENDMENT UNDER 37 C.F.R. §1.111
U.S. Appln. No. 10/057,561

A8275

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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Date: January 29, 2003

APPENDIX
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification is changed as follows:

At page 2, the paragraph encompassing lines 1-8 is amended as follows:

Several strains of *Actinosynnema* have been deposited, such as ATCC ~~31565~~³¹⁵⁶⁵¹, *Actinosynnema pretiosum* subsp. *auranticum*. The metabolic, physiological and maytansinoid ~~maytansanoid~~-producing properties of ATCC 31565 are described in U.S. Patents 4,331,598 and 4,450,234 to Hasegawa et al., issued on May 25, 1982, and May 22, 1984, respectively. ATCC 31565 is a gram-positive bacterium that is capable of growth on a wide range of carbon sources and which produces principally a mixture of maytansinoids and of C-14-hydroxymethyl substituted maytansinoids that may be harvested from the growth medium in low yield.

At page 6, the paragraph encompassing lines 13-16 is amended as follows:

The *Actinosynnema pretiosum* strain of the present invention, herein PF4-4, was deposited under the provisions of the Budapest Treaty with the American Type Culture Collection, 10801 University Blvd., Manassas, Virginia 20110-2209~~Rockville Maryland~~, on December 11, 2001, and has been accorded Accession No. ATCC PTA-3921.

IN THE CLAIMS:

The claims are amended as follows:

1. (Amended) A bacterium having the biological characteristics of the bacterium having deposited with the ATCC on December 11, 2001, under the accession number PTA-3921.

Claims 5-49 are added as new claims.